UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,310	03/14/2001	Samir Khleif	15280415100	9099

20350 7590 02/06/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
DIBRINO, MARIANNE NMN	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,310	KHLEIF ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-8 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2/3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment and response filed 7/17/03 is acknowledged and has been entered.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed method for eliciting an immune response in a subject comprising administering any peptide or protein antigen, including those recited in the instant claims and including from HIV proteins, and further comprising one or more T cell epitopes coordinately with a non-viral vector comprising a polynucleotide encoding a T cell costimulatory molecule, including those antigens, polynucleotides and vectors such as naked DNA vector, recited in the instant claims.

The instant claims encompass use of nucleic acid molecules, polynucleotides, encoding T cell co-stimulatory molecules and further comprising any peptide or protein antigens. There is insufficient disclosure in the specification on such a method as claimed in the instant claims.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

The specification discloses that a secondary "co-stimulation" signal is required for optimal stimulation and effective antigen specific clonal expansion of lymphocytes in addition to a primary antigen specific signal (page 3 at lines 17-19). The specification discloses that T cell co-stimulation is thought to be provided by one or more distinct cell surface molecules expressed by APC, and is thought to involve binding of co-stimulatory molecules on the surface of APC to a corresponding T cell ligand (page 3 at lines 30-33 and continuing on to page 4 at lines 1-10). The specification further discloses B7-1, B7-2, B7-3, B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3 are co-stimulatory molecules (especially page 7 at lines 17 and 18). The specification discloses immunizing mice with a peptide antigen emulsion, i.e., an HPV E7 peptide, followed by an intradermal injection of B7-encoding DNA plasmid vector (especially Example 1). The specification further discloses measuring CTL extracted, i.e., ex vivo, from the said mice for immunoreactivity to the E7 immunizing peptide and an increased effect when B7-encoding DNA plasmid vector was coordinately administered with the peptide antigen. The instant specification does not disclose treatment of subjects with peptide antigens other than the aforementioned HPV E7 peptide antigen and a non-viral vector encoding a costimulatory molecule other than B7.1.

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "T cell co-stimulatory molecule" without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of being able to bind to a T cell ligand and provide a second signal for optimal stimulation of the primary antigen specific signal. It does not specifically define any of the molecules that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than that they bind to a T cell ligand of undisclosed structure. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by the property of binding to an undisclosed T cell ligand and providing a second signal does not suffice to define the genus because it is only an indication of what the property T cell co-stimulatory molecule has. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

The instant disclosure of B7-1, B7-2, B7-3, B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3 does not adequately describe the scope of the claimed invention, which encompasses a substantial variety of subgenera. Since the disclosure fails to provide sufficient relevant identifying characteristics that identify members of the genus, and given the broad genus claimed, the disclosure of a few molecules of defined sequence is insufficient to describe the claimed genus.

Applicant's arguments in the amendment filed 7/17/03 have been fully considered but are not persuasive for the reasons enunciated in the instant rejection. Applicant's arguments are of record in the said amendment.

4. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to elicit an immune response in a subject comprising administering any peptide or protein antigen, including those recited in the instant claims and including those from HIV proteins, comprising one or more T cell epitopes coordinately with a non-viral vector comprising a polynucleotide encoding a T cell co-stimulatory molecule, including those antigens, polynucleotides and vectors such as naked DNA vector, recited in the instant claims. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a method of administering a nucleic acid molecule non-viral vector comprising a polynucleotide encoding a T cell co-stimulatory molecule and further comprising any peptide or protein antigen, including those from HIV, i.e., a method for vaccination against HIV.

The specification discloses that a secondary "co-stimulation" signal is required for optimal stimulation and effective antigen specific clonal expansion of lymphocytes in addition to a primary antigen specific signal (page 3 at lines 17-19). The specification discloses that T cell co-stimulation is thought to be provided by one or more distinct cell surface molecules expressed by APC, and is thought to involve binding of co-stimulatory molecules on the surface of APC to a corresponding T cell ligand (page 3 at lines 30-33 and continuing on to page 4 at lines 1-10). The specification further discloses B7-1, B7-2, B7-3, B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3 are co-stimulatory molecules (especially page 7 at lines 17 and 18). The specification discloses immunizing mice with a peptide antigen emulsion, i.e., an HPV E7 peptide, followed by an intradermal injection of B7-encoding DNA plasmid vector (especially Example 1). The specification further discloses measuring CTL extracted, i.e., ex vivo, from the said mice for immunoreactivity to the E7 immunizing peptide and an increased effect when B7-encoding DNA plasmid vector was coordinately administered with the peptide antigen. The instant specification does not disclose treatment of subjects with peptide antigens other than the aforementioned HPV E7 peptide antigen and a non-viral vector

encoding a costimulatory molecule other than B7.1. The instant specification does not disclose T cell co-stimulatory molecules other than B7-1, B7-2, B7-3, B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3.

Evidentiary reference US Patent No. 5,942,607 (Applicant's IDS reference "AE" in the form 1449 filed 2/3/03) discloses that costimulation is thought to be provided by one or more distinct cell surface molecules expressed by APC, and discloses that B7 is thought to be one such costimulatory molecule (especially column 1 at lines 23-46). There is insufficient guidance in the specification as to how to make and/or use the non-viral vector comprising a polynucleotide encoding a T cell co-stimulatory molecule.

Evidentiary reference Letvin (J. Clin. Investigation 109: 15-20, 2002) teaches that the AIDS vaccine is still a goal, not a reality, and further teaches impediments to HIV vaccine development include the following. "The universal persistence of viral replication in spite of potent immune responses raises the spector that o vaccine-elicited immune response may be capable of fully eliminating or containing indefinitely the replication of HIV." (especially page 15, column 2, 2nd paragraph). Letvin teaches that absence of CTL responses to subunit vaccines in clinical trials (especially Table 1 and page 17, column, first paragraph), that the ultimate configuration of an effective HIV vaccine remains uncertain, but there is a growing consensus that it will require more than a single vaccine modality. "...even a CTL-based vaccine is likely to make use of two distinct vaccine modalities" (especially page 19, column 1, first paragraph). Letvin teaches viral mutations allowing escape from CTL recognition as a limitation of a vaccine approach based solely on the elicitation of CTLs (especially page 19, last paragraph). Evidentiary reference PROMT Accession No. 1998: 555242 (Lancet 24 Oct. 1998, pp 1323(1)) teaches virus variability is an important problem facing HIV vaccine researchers, that researchers have very little idea about what constitutes protective immunity, which animal model is best suited to test vaccine candidates, and that the gap between a vaccine candidate and product development remains vast and ethical concerns surrounding clinical trials have yet to be resolved

There is insufficient guidance in the specification as to how to practice the method of the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments in the amendment filed 7/17/03 are moot in light of the new rejection enunciated supra.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,738,852 (of record) in view of WO 98/04705 (document and CAPLUS Accession No. 1998: 106018 summary of document, of record) and Kaufmann et al (Cell. Immunol. 1996, 169/2 246-251, of record) and further in view of admissions in the specification on page 37 at lines 7-18.

U.S. Patent No. 5,738,852 discloses inducing partial immunity by administering recombinant polynucleotides, including in the form of non-viral vectors or naked DNA or RNA operably linked to regulatory elements for expression, encoding immunostimulatory factor such as B7.1 and/or a target antigen polypeptide from a viral protein (entire document, especially Abstract, claims, column 4 at lines 45-67, column 6 at lines 31-32, column 9 at lines 40-46, column 10 at lines 36-46, column 13 at lines 41-67. U.S. Patent No. 5,738,852 discloses administration by any suitable means known in the art including by parenteral means, i.e., such as "subcutaneous" recited in instant claim 15. U.S. Patent No. 5,738,852 discloses that separate polynucleotides can encode the antigenic polypeptide and the costimulatory molecule, each is mixed with a suitable excipient and the number and timing of doses is determined by routine methods known to those of skill in the art.

U.S. Patent No. 5,738,852 does not disclose administering the viral antigen as a peptide or protein antigen coordinately with the polynucleotide encoding the costimulatory molecule and does not disclose a viral antigen from HPV.

WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the said document teach a pharmaceutical composition for treating a HPV infection comprising HPV E7 polypeptides and a costimulatory molecule B7.1 or a recombinant vector encoding the polypeptides.

Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of costimulatory molecules such as CD80 (B7.1).

The admission in the specification on page 37 at lines 7-18 is that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long term expression of the protein encoded by the DNA. Applicant discloses prior art references at lines 14-18.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the viral polypeptide(s) including the HPV E7 polypeptide taught by Kaufman et al and a costimulatory molecule, such as B7.1 taught by Kaufman et al, U.S. Patent No. 5,738,852 and WO 98/04705 and the CAPLUS Accession No. 1998: 106018, as recombinant polynucleotides as disclosed by U.S. Patent No. 5,738,852 or as polypeptides as taught by WO 98/04705 and the CAPLUS Accession No. 1998: 106018 or as combination of polypeptide antigen and polynucleotide encoding costimulatory molecule or visa versa. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the viral polypeptide(s) either simultaneously or sequentially with the polynucleotide encoding the costimulatory molecule especially given the prior art admission on page 37 at lines 7-18 of prior art that teaches that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long term expression of the protein encoded by the DNA.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because U.S. Patent No. 5,738,852 discloses that the vaccines can be administered as polynucleotides and WO 98/04705 and the CAPLUS Accession No. 1998: 106018 teach that the vaccines can be disclosed as either polynucleotides or as peptides to achieve the common function of eliciting immunity to the viral polypeptide(s) and the prior art admission in the specification teaches that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long term expression of the protein encoded by the DNA.
In addition, Kaufman teaches that response to HPV E7 polypeptide antigen requires expression of costimulatory molecule B7.1. One of ordinary skill in the art at the time the invention was made would have been motivated to administer simultaneously or sequentially depending upon the excipients required for the antigen and the costimulatory molecule or the amounts required per dosage. With regard to the inclusion of claim 8 in the instant rejection, the minimal peptide epitope that binds to an HLA class I molecule to induce a CTL response is from 8-11 amino acid residues in length; for example, peptides that bind to HLA-A2.1 a common HLA molecule in the Caucasians, are a minimum 9 amino acid residues in length.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07.

It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Instant claim 15 is included in this rejection because it would have been prima facie obvious at the time the invention was made to have administered the antigen and polynucleotide "to proximal target sites selected from the same, or closely adjacent...sites" depending upon what route was desired. In addition, the limitation "closely adjacent" can be broadly interpreted to read on sites of undetermined distance.

Applicant's arguments in the amendment filed 7/17/03 have been fully considered but are not persuasive for the reasons enunciated in the instant rejection. Applicant's arguments are of record in the said amendment.

7. Claims 1, 2, 6 and 11-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,245,525 in view of admissions in the specification on page 37 at lines 7-18.

U.S. Patent No. 6,245,525 discloses administration of peptide or protein antigens and costimulatory molecules in vaccination protocols as either protein or nucleic acid forms, including administering the B7-1 costimulatory molecule as naked DNA and further comprising pharmaceutically acceptable carriers for the induction of CTL responses and using various routes of administration including subcutaneous (especially column 32 at lines 11-61 and column 35 at lines 33-60). U.S. Patent No. 6,245,525 discloses peptides that bind to HLA class I molecules are a minimum of 9 amino acid residues in length (especially column 19 at Table 1).

U.S. Patent No. 6,245,525 does not disclose administration of a peptide or protein antigen coordinately with a non-viral vector comprising a polynucleotide encoding a T cell costimulatory molecule.

The admission in the specification on page 37 at lines 7-18 is that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long term expression of the protein encoded by the DNA. Applicant discloses prior art references at lines 14-18.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the peptide or protein antigen disclosed by U.S. Patent No. 6,245,525 coordinately with the nucleic acid form of the B7 costimulatory molecule, such as naked DNA encoding B7 disclosed by U.S. Patent No. 6,245,525 and as taught by the said prior art admissions in the instant specification for injection and subsequent long term expression of the protein encoded by DNA when injected as naked DNA.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to induce an immune response to the protein or peptide antigen. In addition, one of ordinary skill in the art at the time the invention was made would have been motivated to administer simultaneously or sequentially depending upon the excipients required for the antigen and the costimulatory molecule or the amounts required per dosage.

Instant claim 15 is included in this rejection because it would have been prima facie obvious at the time the invention was made to have administered the antigen and polynucleotide "to proximal target sites selected from the same, or closely adjacent...sites" depending upon what route was desired. In addition, the limitation "closely adjacent" can be broadly interpreted to read on sites of undetermined distance.

8. Claims 7 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S . Patent No. 6,245,525 in view of admissions in the specification on page 37 at lines 7-18 as applied to claims 1, 2, 6 and 11-17 above, and further in view of WO 98//04705 (and the CAPLUS Accession No. 1998: 106018 summary of the said document, of record) and Kaufmann et al (Cell. Immunol. 1996, 169/2 246-251, of record).

U.S. Patent No. 6,245,525 and the prior art admissions in the specification on page 37 at lines 7-18 have been discussed supra (hereafter "the combined references").

The combined references do not teach wherein the protein or peptide antigen is from HPV.

WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the said document teach a pharmaceutical composition for treating a HPV infection comprising HPV E7 polypeptides and a costimulatory molecule B7.1 or a recombinant vector encoding the polypeptides.

Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of costimulatory molecules such as CD80 (B7.1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted an HPV protein or peptide antigen comprising one or more T cell epitopes into the composition taught by the combined references particularly since WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the said document teach a pharmaceutical composition for treating a HPV infection comprising HPV E7 polypeptides and a costimulatory molecule B7.1 or a recombinant vector encoding the polypeptides and Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of costimulatory molecules such as CD80 (B7.1).

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat HPV infection as taught by WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the said document because the need for treatment

and effective CTL response is taught by Kaufman et al, the lack of effective CTL response to HPV due to a lack of expression of costimulatory molecules such as CD80 (B7.1) is taught by Kaufman et al and US Patent No. 5,738,852 discloses that polynucleotides can encode antigenic polypeptides and costimulatory molecules for induction of an effective immune response.

9. The references crossed out in the Form 1449 filed 2/3/03 have not been considered because they can't be located or Applicant has not provided copies. They will be considered in the next Office Action. It would expedite prosecution if Applicant would send in copies of references.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842). The Examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan, can be reached at 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 (before final) or 703-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
January 23, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600